

Notice of Allowability

Application No.

09/255,397

Examiner

Ram Shukla

Applicant(s)

SERBEDZIJA ET AL.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address--

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance and Issue Fee Due or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. ☒ This communication is responsive to 4-25-01.
2. ☒ The allowed claim(s) is/are 91-116.
3. ☐ The drawings filed on _____ are acceptable as formal drawings.
4. ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) ☐ All b) ☐ Some* c) ☐ None of the:
 1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).
- * Certified copies not received: _____.
5. ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application. **THIS THREE-MONTH PERIOD IS NOT EXTENDABLE FOR SUBMITTING NEW FORMAL DRAWINGS, OR A SUBSTITUTE OATH OR DECLARATION. This three-month period for complying with the REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL is extendable under 37 CFR 1.136(a).**

6. ☐ Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient. A SUBSTITUTE OATH OR DECLARATION IS REQUIRED.
7. ☒ Applicant MUST submit NEW FORMAL DRAWINGS
 - (a) ☒ including changes required by the Notice of Draftsperson's Patent Drawing Review(PTO-948) attached
 - 1) ☒ hereto or 2) ☐ to Paper No. 16.
 - (b) ☐ including changes required by the proposed drawing correction filed _____, which has been approved by the examiner.
 - (c) ☐ including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No. _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings. The drawings should be filed as a separate paper with a transmittal letter addressed to the Official Draftsperson.

8. ☐ Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Any reply to this letter should include, in the upper right hand corner, the APPLICATION NUMBER (SERIES CODE / SERIAL NUMBER). If applicant has received a Notice of Allowance and Issue Fee Due, the ISSUE BATCH NUMBER and DATE of the NOTICE OF ALLOWANCE should also be included.

Attachment(s)

- | | |
|--------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------|
| 1 <input type="checkbox"/> Notice of References Cited (PTO-892) | 2 <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3 <input checked="" type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 4 <input checked="" type="checkbox"/> Interview Summary (PTO-413), Paper No. <u>15</u> |
| 5 <input type="checkbox"/> Information Disclosure Statements (PTO-1449), Paper No. _____ | 6 <input checked="" type="checkbox"/> Examiner's Amendment/Comment |
| 7 <input type="checkbox"/> Examiner's Comment Regarding Requirement for Deposit of Biological Material | 8 <input checked="" type="checkbox"/> Examiner's Statement of Reasons for Allowance |
| | 9 <input type="checkbox"/> Other |

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EXAMINER'S AMENDMENT

1. An examiner's amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 CFR 1.312. To ensure consideration of such an amendment, it MUST be submitted no later than the payment of the issue fee.

Authorization for this examiner's amendment was given in a telephone interview with Mr. Joe Liebeschuetz on 4-25-01.

2. The application has been amended as follows:

IN THE CLAIMS:

Claims ~~1-21~~, ~~54-74~~, and ~~80-88~~ have been canceled.

New claims 91-116 have been added.

~~1-91~~ A method of screening a candidate agent for an effect on cell death activity, said method comprising in the following order:

(a) contacting a living teleost post 12-hours of development with a dye wherein said dye has an affinity for dead cells and wherein said dye stains dead cells;

(b) administering the candidate agent to the living teleost;

(c) detecting the staining of dead cells with said dye in at least one specific tissue or organ in the living teleost;

(d) comparing the staining of dead cells with said dye in said at least one specific tissue or organ of the living teleost with the staining of dead cells with said dye in said at least one specific tissue or organ of a control living teleost that was not administered said candidate agent;

wherein an increase or decrease in the staining of dead cells with said dye in the treated living teleost compared to the control living teleost would indicate the effect of the candidate compound on cell death activity.

~~2~~
~~92~~ The method of claim ~~91~~, wherein the effect is an increase in cell death activity.

~~3~~
~~93~~ The method of claim ~~92~~, wherein the method further comprises detecting a change in cell death activity in the living teleost after a predetermined period of time, wherein

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said predetermined period of time is sufficient for a detectable difference in cell death activity to occur in presence of the candidate agent.

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~~94~~. The method of claim ³~~93~~, wherein the method further comprises detecting the increase in cell death activity over time at predetermined intervals.

⁵
~~95~~. The method of claim ²~~92~~, wherein the increase in cell death activity is detected in more than one tissue or organ of the living teleost simultaneously.

⁶
~~96~~. The method of claim ⁵~~95~~, wherein the increase in cell death activity is detected in more than one tissue or organ of the living teleost simultaneously over time at predetermined intervals.

⁷
~~97~~. The method of claim ¹~~91~~, wherein the effect is a decrease in cell death activity.

⁸
~~98~~. The method of claim ¹~~91~~, wherein the effect is an increase in apoptotic activity or necrotic activity.

⁹
~~99~~. The method of claim ⁸~~98~~, wherein the increase in apoptotic activity comprises an increase in cell death in said at least one specific tissue or organ of the living teleost.

¹⁰
~~100~~. The method of claim ⁸~~98~~, wherein the increase in apoptotic activity is detected by light microscopy or fluorescence microscopy.

¹¹
~~101~~. The method of claim ⁸~~98~~, wherein the increase in apoptotic activity or necrotic activity is detected in at least one specific organ or tissue.

¹²
~~102~~. The method of claim ¹~~91~~, wherein the effect is a decrease in apoptotic activity or necrotic activity.

¹³
~~103~~. The method of claim ¹²~~102~~, wherein the decrease in apoptotic activity comprises a decrease in cell death in said at least one specific tissue or organ of the living teleost.

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¹⁴
~~104~~. The method of claim ¹~~91~~, wherein the candidate agent is administered to the living teleost by dissolving the candidate agent in culture media containing the living teleost.

¹⁵
~~105~~. The method of claim ¹~~91~~, wherein a fluorescent dye which labels dead or dying cells is administered to the teleost prior to administration of the candidate agent to the living teleost.

¹⁶
~~106~~. The method of claim ¹⁵~~105~~, wherein the fluorescent dye is administered to the living teleost by dissolving the fluorescent dye in media containing the living teleost.

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~~107~~. The method of claim ¹⁵~~105~~, wherein the fluorescent dye is administered to the living teleost by injecting the fluorescent dye into the living teleost.

¹⁸
~~108~~. The method of claim ¹⁵~~105~~, further comprising administering the candidate agent to the living teleost by dissolving the candidate agent in the culture media containing the living teleost or injecting the candidate agent into the living teleost after administration of the fluorescent dye to the living teleost.

¹⁹
~~109~~. The method of claim ¹⁵~~105~~, wherein a fluorescent dye is a monomeric cyanine dye.

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~~110~~. The method of claim ¹⁹~~109~~, wherein the fluorescent dye is benzothiazolium-4-quinolium dye.

²¹
~~111~~. The method of claim ¹~~91~~, wherein the living teleost is a zebrafish.

²²
~~112~~. The method of claim ¹~~91~~, wherein the candidate agent is a compound and a library of compounds is screened for an effect on cell death activity.

²³
~~113~~. The method of claim ¹~~91~~, further comprising screening the candidate agent for a toxic activity.

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²⁴
114. The method of claim ¹91, wherein the method is conducted in a living teleost in vivo.

²⁵
115. The method of claim ¹91, wherein the living teleost is contained in a microtiter well.

²⁶
116. The method of claim ¹91, wherein the dye in said at least one specific tissue or organ is detected using a microplate reader. --

3. The following is an examiner's statement of reasons for allowance:

The claimed invention is free of the prior art of record the prior art of record does not teach or fairly suggest using a living teleost post 12 hours of development in screening for candidate agents that alter cell death activity, wherein a dye to stain dead cells is contacted to the living teleost before the candidate agents are administered to the living teleost .

Any comments considered necessary by applicant must be submitted no later than the payment of the issue fee and, to avoid processing delays, should preferably accompany the issue fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Kay Pinkney whose telephone number is (703) 305-3553.

Ram R. Shukla, Ph.D.

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